UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/411,006	10/01/99	TYE	R 07907.0002US

EXAMINER	
GUPTA, A	
ART UNIT	**PAPER NUMBER**
1653	8

022930 HM12/0327
HOWREY SIMON ARNOLD & WHITE LLP
BOX 34
1299 PENNSYLVANIA AVENUE NW
WASHINGTON DC 20004

DATE MAILED: 03/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

. Office Action Summary	Application No. 09/411,006	Applicant(s) Tye, R.
	Examiner ANISH GUPTA	Group Art Unit 1653

☒ Responsive to communication(s) filed on *Jan 17, 2001*

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-71* is/are pending in the application.

Of the above, claim(s) *65-71* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-64* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I in Paper No. 7 is acknowledged. Claims 1-64 have been examined in this application and an office action follows below.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 20-26, 28-34, 36-41, 43-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20, 28, 36, 43, 52, 59 recite that oxygen is removed by centrifuging the red blood cells under vacuum sufficient to remove oxygen form the preparation. However, it is unclear if the centrifuging of the blood cells or the vacuum of the blood cells yields the removal of oxygen. Thus, one can not determine if a certain speed is necessary to remove the oxygen if the centrifuge is responsible for the removal of oxygen. Furthermore, it is unclear what is defined as "sufficient" for the removal of oxygen.

In claim 36 and 43, there are two periods at the end of the sentence, correction is requested.

For methods drawn to a method of increasing the oxygen carrying capacity of an individual, it is unclear to what the oxygen carrying capacity is being measured against. Does the individual have lower oxygen carrying capacity relative to another individual, or does the individual have increased oxygen carrying capacity relative to him/herself, prior to the administration of the hemoglobin. Accordingly, the claims are indefinite and it is unclear from the claims as to what "individual" the hemoglobin is administered to.

Claim 23, 31, 39, 46, 55, 62 all recite "a speed sufficient to produce a force greater than the surface tension of the solution." However, there is no antecedent basis for the phrase "the solution" in the base claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-18, 27, 29, 32-34, 42, 44, 47-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Tye et al.

The claims are drawn to a non pyrogenic, endotoxin free, oxygen free, stroma free, cross-linked hemoglobin, cross linked with bis dibromo salicyl fumarate and modified by pyridoxal-5'-phosphate.

The reference teach a stroma free tense state tetrameric hemoglobin cross linked with bis(3,5-dibromosalicyl)-fumarate and modified with pyridoxal-5'-phosphate (see claim 1 and 3 of the patent). The modified hemoglobin serves as a blood substitute product with a storage life of greater than two years (see col. 6, lines 50-64). Further, the modified hemoglobin has "superior oxygen transport capabilities not found in stroma free hemoglobin" (see col. 7, lines 5-11). The method of making the modified hemoglobin involves the isolation of hemoglobin, subjecting the solution to a vacuum and flushing with inert gas until the oxygen tension is decreased at a value of 1.0mm Hg, reacting with bis(3,5-dibromosalicyl)-fumarate (BDBF), finally modifying with pyridoxal-5'-phosphate (see col. 9, lines 39-68 and col. 10, lines 1-36). The source of the hemoglobin can include human, bovine, bovine, or porcine (see col. 8, lines 17-20). Note that claims 47-64 are drawn to a product by process. The reference mees the claimed limitation of a non pyrogenic, endotoxin free, oxygen free, stroma free, cross-linked hemoglobin, cross linked with bis dibromo salicyl fumarate and modified by pyridoxal-5'-phosphate. However, the courts have held that "[t]he patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tye in view of Bucci et al.

The claims are drawn to a non pyrogenic, endotoxin free, oxygen free, stroma free, cross-linked hemoglobin, cross linked with bis dibromo salicyl fumarate and modified by pyridoxal-5'-phosphate.

The reference of Tye et al. has been discussed supra. The difference between the prior art and the instant application is that the reference does not teach removing endotoxin from preparation containing red blood cells, removing oxygen from red blood cells, and lysing red blood cells.

However, Bucci et al. states that it is necessary to have the hemoglobin in deoxy form for the pyridoxylation with pyridoxal-5'-phosphate (see col. 3, lines 58-62). The reference teach various methods for deoxygenation hemoglobin prior to pyridoxylation. One method involves the suspension of red blood cells with a reducing agent to maintain the solution in deoxy form (see col. 3, lines 50-64). The solution with the red blood cells are then subjected to a heating step that lyses the cells and extracts the free reduced hemoglobin (see col. 3, lines 65-68). Before the polymerization, the solution is subject to precipitation and centrifugation to remove all of the organic and inorganic material from hemoglobin (see col. 5, lines 57-64). The reference further states that the reducing agent maintains the environment oxygen free. Moreover, although not necessary, an atmosphere of an inert, oxygen free gas may be present, such as nitrogen or argon. The reference states, however, the "necessary reaction condition in this respect maintaining an oxygen free atmosphere] can easily be determined by a person skilled in the art" (see col. 4, lines 53-68 and col. 5, lines 39-44). Note that Tye teach that the environment can be maintained oxygen free by purging the environment with an inert gas and removing the gas by vacuum (see Tye col. 10, lines 3-5). Finally, Bucci et al. teach that the starting material can also be blood cells which have been subject to lysis and from which the stroma has been removed completely or partially (see col. 3, lines 43-46). The reference mees the claimed limitation of a non pyrogenic, endotoxin free, oxygen free, stroma free, cross-linked hemoglobin, cross linked with bis dibromo salicyl fumarate and modified by pyridoxal-5'-phosphate. Therefore, it would have been obvious to one of ordinary skill in the art to utilize

the method disclosed in Bucci et al. to maintain the hemoglobin in deoxygenated from because deoxy-hemoglobin is necessary for polymerization to occur.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can normally be reached on (703)308-2923. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Anish Gupta